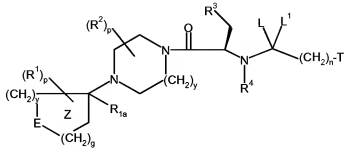
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in this application:

1. (Currently Amended) A compound of formula I:



(I)

or a pharmaceutically acceptable salt, or stereoisomer thereof,

wherein:

L and L^1 combine together to form an oxo group;

E is: O, S, NR^{1b}, SO, SO_2, CR^9, or $C(R^9)_2$ wherein R^9 combines with ~~and~~ an adjacent R^1 to form a 5, 6, or 7-member saturated or unsaturated carbocycle;

wherein the Z ring has ~~0,~~ or 1 double bond between the $C(R^9)$ carbon and an adjacent carbon attached to R^1;

R^1 is selected from the group consisting of:

hydrogen, and

C_1-C_8 alkyl,

R_{1a} is hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

(D)aryl,

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, and aryl~~l~~ are optionally substituted with one to five substituents independently selected from the group consisting of halo, hydroxy,

C_1-C_8 alkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl; provided that halo and hydroxy groups are not substituted on a carbon atom adjacent to a heteroatom;

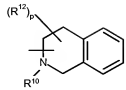
R^{1b} is: hydrogen,
C_1-C_8 alkyl,
(D)C_3-C_7 cycloalkyl,
SO_2(C_1-C_8 alkyl),
(D)C(O)C_1-C_4 alkyl,
(D)C(O)OC_1-C_4 alkyl, or
SO_2(D)phenyl, wherein the phenyl group is optionally substituted with one to five substituents selected from halo, and C_1-C_8 alkyl;

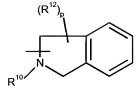
R^2 is: hydrogen, or
C_1-C_8 alkyl;

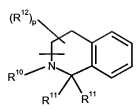
R^3 is: phenyl, aryl or thienyl;
wherein phenyl, aryl and thienyl are optionally substituted with one to three substituents independently selected from the group consisting of:
cyano, perfluoroC_1-C_4 alkoxy, halo, C_1-C_8 alkyl, (D)C_3-C_7 cycloalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl;

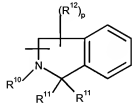
R^4 is: hydrogen,
C_1-C_8 alkyl,

T is:









R^9 is independently:

hydrogen,

(C_1-C_8) alkyl,

C_2-C_8 alkenyl,

C(O)C_1-C_8 alkyl, or

phenyl,

R^{10} is: hydrogen,

(C_1-C_8) alkyl,

C(O)C_1-C_8 alkyl, or

phenyl,

R^{11} is independently:

hydrogen, (C_1-C_8) alkyl, (D)phenyl, or aryl;

R^{12} is independently:

C_1-C_8 alkyl,

phenyl,

aryl;

D is: a bond or C_1-C_4 alkyl;

g is: 0, 1, or 2;

y is: 1 ~~and;~~

n is: 0-8; and

p is 0-4.

2. (Canceled)

3. (Original) The compound according to Claim 1 wherein the Z ring is saturated.

4. (Canceled)

5. (Previously Presented) The compound according to Claim 3 wherein E is O, S, NR^{1b}, or SO_2.

6. (Canceled)

7. (Canceled)

8. (Previously Presented) The compound according to Claim 1 wherein for the Z ring R^1 is hydrogen.

9-10. (Canceled)

11. (Currently Amended) The compound according to Claim 10 wherein ~~R^{1a}~~ R_{1a} is isopropyl, isobutyl, cyclohexylmethyl, phenyl, 2-fluorobenzyl or benzyl.

12. (Previously Presented) The compound according to Claim 1 wherein E is selected from the group consisting of: $-NCH_3$, $-NCH(CH_3)_2$, S, CR^9, $C(R^9)_2$, $-NCH_2CH_3$, and O.

13. (Previously Presented) The compound according to Claim 12 wherein E is $C(R^9)_2$, wherein one R^9 is selected from hydrogen and C_1-C_4 alkyl, and the other R^9 combines with an adjacent R^1 to form a 5 or 6-member carbocycle.

14. (Previously Presented) The compound according to Claim 1 wherein R^2 is hydrogen.

15. (Previously Presented) The compound of Claim 1 wherein R^3 is phenyl optionally being para-substituted with chloro, bromo, methoxy or methyl.

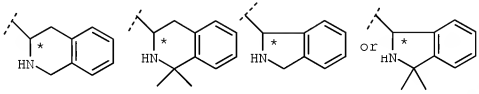
16. (Previously Presented) The compound of Claim 15 wherein R^3 is phenyl para-substituted with chloro.

17. (Previously Presented) The compound of Claim 1 wherein R^{10} is hydrogen, C_1-C_4 alkyl, or $C(O)C_1$-C_4 alkyl.

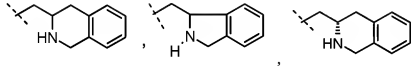
18. (Previously Presented) The compound of Claim 17 wherein R^{10} is hydrogen at each occurrence.

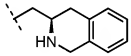
19. (Canceled)

20. (Previously Presented) The compound according to Claim 1 wherein "T" is a moiety of the formula:



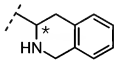
21. (Previously Presented) The compound according to Claim 1 wherein "T" is a moiety selected from the group consisting of:





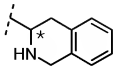
and .

22. (Previously Presented) The compound of Claim 1 wherein T is a moiety of the formula:



wherein the carbon atom marked * represents a chiral center.

23. (Previously Presented) The compound of Claim 1 wherein L and L^1 are each hydrogen; and T is a moiety of the formula:



24. (Canceled)

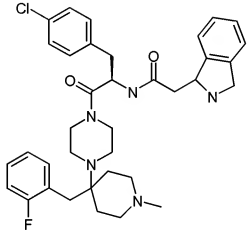
25. (Canceled)

26. (Canceled)

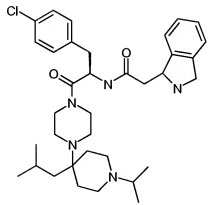
27. (Previously Presented) A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutical carrier.

28. (Withdrawn - Currently Amended) The pharmaceutical composition of Claim 27 further comprising a second active ingredient selected from the group consisting of an insulin sensitizer, insulin mimetic, sulfonylurea, alpha-glucosidase inhibitor, HMG-CoA reductase inhibitor, sequestrant cholesterol lowering agent, beta 3 adrenergic receptor agonist, neuropeptide Y antagonist, phosphodiester V inhibitor, and an ~~alpha2~~ alpha 2 adrenergic receptor antagonist.

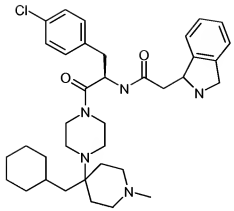
29. (Currently Amended) A compound selected from the group consisting of:



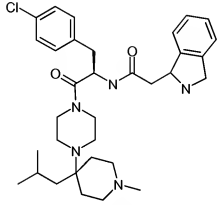
N-(1-(4-Chloro-benzyl)-2-{4-[4-(2-fluoro-benzyl)-1-methyl-piperidin-4-yl]-piperazin-1-yl}-2-oxo-ethyl)-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



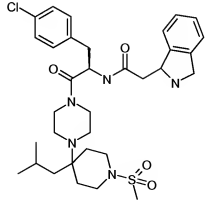
N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-1-isopropyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



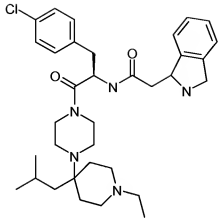
N-{1-(4-Chloro-benzyl)-2-[4-(4-cyclohexylmethyl-1-methyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



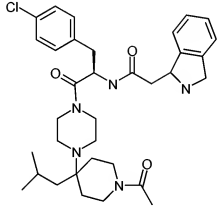
N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-1-methyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



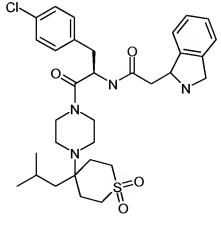
N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-1-methanesulfonyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



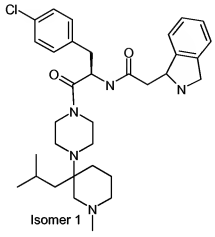
N-{1-(4-Chloro-benzyl)-2-[4-(1-ethyl-4-isobutyl-piperidin-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



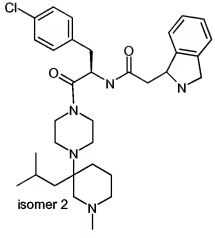
N-[2-[4-(1-Acetyl-4-isobutyl-piperidin-4-yl)-piperazin-1-yl]-1-(4-chloro-benzyl)-2-oxo-ethyl]-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



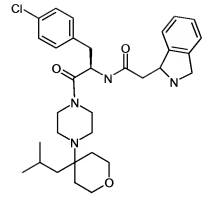
N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-1,1-dioxo-hexahydro-1l6-thiopyran-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



N-{1-(4-Chloro-benzyl)-2-[4-(3-isobutyl-1-methyl-piperidin-3-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,

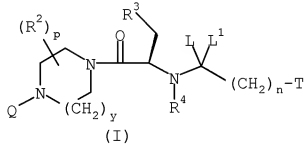


N-{1-(4-Chloro-benzyl)-2-[4-(3-isobutyl-1-methyl-piperidin-3-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide,



N-{1-(4-Chloro-benzyl)-2-[4-(4-isobutyl-tetrahydro-pyran-4-yl)-piperazin-1-yl]-2-oxo-ethyl}-2-(2,3-dihydro-1H-isoindol-1-yl)-acetamide~~, and~~.

30. (Currently Amended) A process for preparing a compound of formula I:

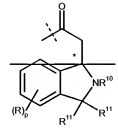


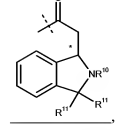
(I)

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

-CLL'-$(CH_2)_n$-T is:





R^{10} is a CBz or Boc protecting group, hydrogen, (C_1-C_8) alkyl, , C(O)C_1-C_8 alkyl, or phenyl,;

Q is represented by the moiety:

,

L and L^1 combine together to form an oxo group;

E is: O, S, NR^{1b}, SO, SO_2, CR^9, or $C(R^9)_2$, wherein R^9 combines with an adjacent R^1 to form a 5, 6, or 7-member saturated or unsaturated carbocycle;

wherein the Z ring has ~~0,~~ or 1 double bond between CR^9 and an adjacent carbon attached to R^1;

R^1 is selected from the group consisting of:

hydrogen, and

C_1-C_8 alkyl,

R_{1a} is: hydrogen.;

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

(D)phenyl,

(D)aryl,

~~(D)heteroaryl;~~

wherein C_1-C_8 alkyl, C_3-C_7 cycloalkyl, phenyl, and aryl ~~and heteroaryl~~ are optionally substituted with one to five substituents independently selected from the group consisting of halo, hydroxy, C_1-C_8 alkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl; provided that halo and hydroxy groups are not substituted on a carbon atom adjacent to a heteroatom;

R^{1b} is: hydrogen,

C_1-C_8 alkyl,

(D)C_3-C_7 cycloalkyl,

SO_2(C_1-C_8 alkyl),

(D)$C(O)C_1$-C_4 alkyl,

(D)$C(O)OC_1$-C_4 alkyl, or

SO_2(D)phenyl, wherein the phenyl group is optionally substituted with one to five substituents selected from halo, and C_1-C_8 alkyl;

R^2 is: hydrogen, or
C_1-C_8 alkyl~~,~~;

R^3 is: phenyl, aryl or thienyl;
wherein phenyl, aryl and thienyl are optionally substituted with one to three substituents independently selected from the group consisting of:
cyano, perfluoroC_1-C_4 alkoxy, halo, C_1-C_8 alkyl, (D)C_3-C_7 cycloalkyl, C_1-C_4 alkoxy, and C_1-C_4 haloalkyl;

R^4 is: hydrogen,
C_1-C_8 alkyl~~,~~;

R^9 is independently hydrogen, (C_1-C_8) alkyl, C_2-C_8 alkenyl, C(O)C_1-C_8 alkyl, or phenyl;

R^{11} is independently:
hydrogen, (C_1-C_8) alkyl, (D)phenyl or aryl;

D is: a bond or C_1-C_4 alkyl;

g is: 0, 1, or 2;

y is: 1;

n is: 0-8; and

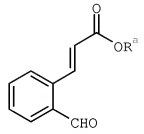
p is 0-4;

comprising the steps of:

a) reacting a compound having a structural formula 1:

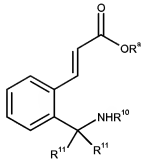
(1)

with $CH_2CH=C(O)OR^a$ wherein R^a is hydrogen or C_1-C_8 alkyl and X is halo, in the presence of a catalyst and a base in a suitable organic solvent to give the compound of formula 2:



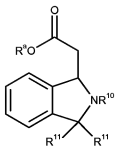
(2);

b) reductively aminating the compound of formula 2 in the presence of amine in an acidic condition to give a compound of formula 3:



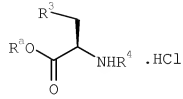
(3);

c) cyclizing the compound of formula 3 by Michael addition to give a compound of formula 4 or stereoisomers thereof:



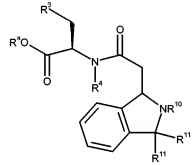
(4);

d) coupling the compound of formula 4 or stereoisomers thereof wherein R^a is H, with a compound of formula 5:



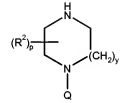
(5);

wherein R^a is C_1-C_8 alkyl, to give a compound of formula 6:



(6); and

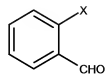
e) coupling the compound of formula 6 wherein R^a is H, with a compound having a structural formula:



,

to afford the compound of formula 1.

31. (Previously Presented) The process of Claim 30, wherein:



in Step a) is 2-bromobenzaldehyde.

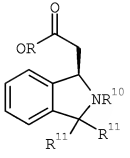
32. (Previously Presented) The process of Claim 30, wherein $CH_2CH=C(O)OR^8$ in Step (a) is methylacrylate.

33. (Previously Presented) The process of Claim 30, wherein the catalyst in Step (a) is selected from the group consisting of: $Pd(Ph_3P)_2Cl_2$, $Pd(Ph_3P)_4Cl_2$, $Pd(Ph_3P)_4$, $Pd(Ph_3P)_2Cl_2$/CuI, $Pd(OAc)_2/Ph_3P$-Bu_4NBr, $Pd(Ph_3P)_4Cl_2/H_2$ and $Pd(OAc)_2/P(O\text{-}tol)_3$; and wherein the base in Step (a) is $N(R)_3$ where R is hydrogen or C_1-C_8 alkyl.

34. (Previously Presented) The process of Claim 30, wherein the amine in Step (b) is selected from the group consisting of: benzylamine, alpha-methylbenzylamine and $BocNH_2$.

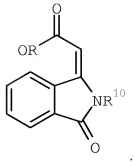
35. (Original) The process of Claim 34, wherein Step (b) further comprises the step of reducing an intermediate imine compound in the presence of reducing agent selected from the group consisting of: $NaCNBH_3$, $Na(OAc)_3BH$, $NaBH_4$/H+ and a combination of Et_3SiH and TFA in CH_3CN or CH_2Cl_2.

36. (Previously Presented) The process of Claim 30, wherein the stereoisomer of compound of formula (4) in Step (c) is a compound of formula 7a:



(7a).

37. (Previously Presented) The process of Claim 36, wherein the compound of formula 7a is prepared by asymmetric hydrogenation of a compound having structural formula,



38. (Previously Presented) The process of Claim 30, wherein the Michael addition in Step (c) is carried out under basic workup condition.

39. (Previously Presented) The process of Claim 30, wherein the Step (e) further comprises deprotecting or protecting the nitrogen of the NR^{10} substituent.

40-43. (Canceled)

44. (Previously Presented) A method of treating obesity in a mammal comprising the administration of a therapeutically effective amount of the compound of formula I as recited in Claim 1.

45-47. (Canceled)